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## **GENERAL**

Kamari Pharma is a biopharmaceutical company aiming to develop and commercialize proprietary small molecule (SMC) inhibitors of TRPV3, a cation channel expressed primarily in keratinocytes, for the treatment of dermatological conditions with unmet need. TRPV3 has been extensively evaluated as a target for drug development, identified as the cause of Olmsted Syndrome in humans, and showing involvement in various skin disorders, including: Keratodermas, Atopic Dermatitis, Psoriasis, Rosacea, post-burn pruritus and others.

Kamari Pharma was established in October 2018 supported by Pontifax and Arkin holdings Ltd.

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## **SCIENTIFIC APPROACH**

Transient receptor potential vanilloid 3 (TRPV3) is a member of the TRP (Transient Receptor Potential) super-family. It is a relatively underexplored member of the thermo-TRP sub-family, TRPV3 is a non-selective cation channel, displaying relatively high permeability to calcium. It was first cloned in 2002 and displays ~30%–40% sequence homology with other TRPV channels. Genetic mutations, use of gene knock-outs and selective pharmacological tools are helping to provide insights into its role and therapeutic potential. TRPV3 is highly expressed in skin, where it is implicated in skin physiology and pathophysiology, thermo-sensing and nociception. Gain of function TRPV3 mutations in rodent and man have enabled the role of TRPV3 in skin health and disease to be particularly well defined. Pre-clinical studies provide some rationale to support development of TRPV3 antagonists for therapeutic application for the treatment of hyperkeratosis, inflammatory skin conditions and itch. However, to date, only one compound directed towards block of the TRPV3 receptor (GRC15300) has progressed into clinical trials for pain (failure in Phase II trial for neuropathic pain). Currently, there are no known clinical trials in progress employing a TRPV3 antagonist. TRPV3 is expressed in epidermal skin keratinocytes across species and in humans, TRPV3 gene expression in skin is the highest of the >50 tissues profiled. In addition, TRPV3 protein has been found throughout the epidermis and around hair follicles, with protein elevated under certain inflammatory skin conditions.

## **INDICATIONS**

TRPV3 activation in keratinocytes has been shown to mediate the release of pro-inflammatory and pro-nociceptive mediators and pruritogens, and the gain-of-function mutations implicate TRPV3 in skin conditions where a predominant feature is itch.

Potential therapeutic utilities of TRPV3 modulators are: Olmsted syndrome, Palmoplantar Keratodermas, Ichthyoses, Pruritic and Atopic Dermatitis, Psoriasis, Wound Healing, Burn/Post-burn pruritus, Hair growth, Skin Barrier Formation, Rosacea and more.